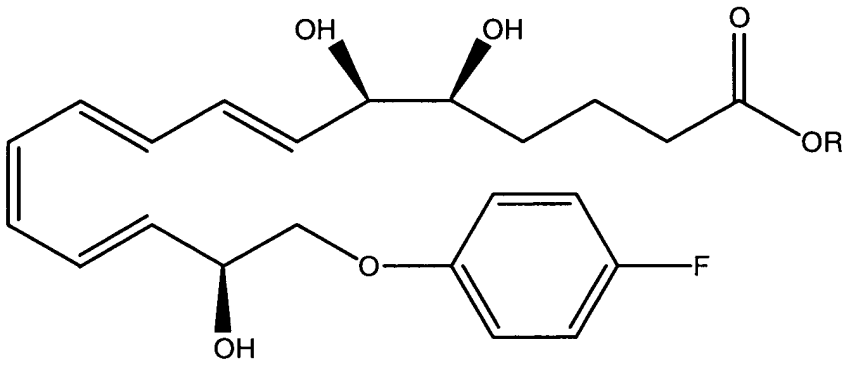
Rejection of claims 17-32 under 35 U.S.C. § 112, Second paragraph

Claims 17-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention because of the variable of R_1 is further defined into itself, as shown in the group "$C(=O)R_1$".

Applicant respectfully asserts that this was an apparent "supercopy" error in the preparation of the Office Action. The pending claims do not include a "$C(=O)R_1$" group. The claims pertain to a lipoxin analog having the formula



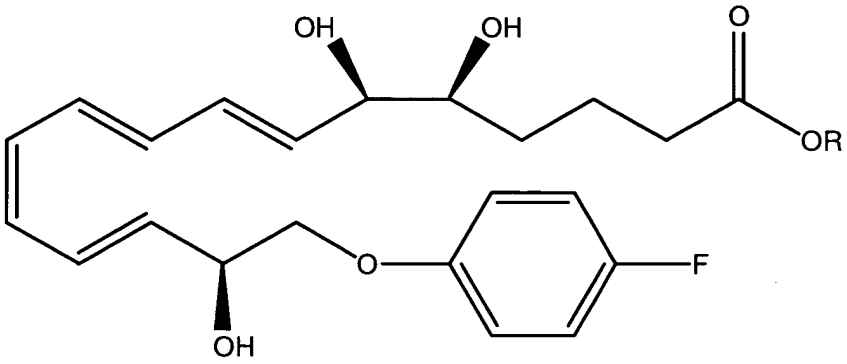
wherein R is a hydrogen atom, a pharmaceutically acceptable ester and pharmaceutically acceptable salts thereof.

Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 17 through 32 under 35 U.S.C. § 103(a)

Claims 17 through 32 are rejected under 35 U.S.C. §103(a) as being unpatentable over "Biochemistry and Cell Biology of Phospholipase D in Human Neutrophils", Chemistry and Physics of Lipids, 80, 3 (1996) (hereinafter "Olson") in view of "Neutrophil-mediated Changes in Vascular Permeability Are Inhibited by Topical Application of Aspirin-triggered 15-epi-lipoxin A_4 and Novel Lipoxin B_4 Stable Analogues" J. Clin. Invest. 101, 819 (1998) (hereinafter "Takano").

The present invention is directed to methods for the modulation of a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation; methods for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation; methods for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity; methods for treatment of PLD initiated superoxide generation or degranulation activity in a subject by the administration of an effective anti-inflammatory amount of a lipoxin analog to the subject. The lipoxin analog has the formula



wherein R is a hydrogen atom, a pharmaceutically acceptable ester and pharmaceutically acceptable salts thereof.

Additionally, the present invention also relates to packaged pharmaceutical compositions which contain the lipoxin analog(s) and instructions to treat the afflictions described above.

Olson describes a ***biochemical pathway*** for receptor-activated phospholipase-D (PLD) in isolated neutrophils and inflammation.

Olson, the primary reference, fails to teach or suggest, provide any motivation or an expectation of success so that one of ordinary skill in the art would utilize ***any therapeutic agent*** to treat a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation or for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation or for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity or for treatment of PLD initiated superoxide generation or degranulation activity.

Olson, the primary reference, simply describes a biochemical pathway involving PLD. Olson, does not identify, teach or suggest, or provide any motivation or suggestion that treatment of this biochemical pathway would interfere, diminish, or alleviate inflammation in any manner. Olson does not offer a solution to the consequences of PLD involvement in any situation including neutrophil recruitment. Olson, at best, invites a researcher to search for a therapeutic agent that would interfere with the biochemical pathway involving PLD. An invitation to experiment, does not in and of itself, provide a basis for teaching, suggesting, or motivating one skilled in the art that a solution to the problem is at hand. Olson, again at best, provides a problem to be solved.

Applicant has identified the problem (regulation of PLD activity and PMN inflammation) and has addressed the problem, regulation of PLD activity, by interfering with the biochemical pathway with unique and nonobvious compounds, i.e., the lipoxin compounds as presently claimed.

Olson also fails to teach or suggest, provide any motivation or an expectation of success so that one of ordinary skill in the art would utilize ***any therapeutic agent*** in ***packaged pharmaceuticals*** with instructions for the treatment of a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation or for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation or for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity or for treatment of PLD initiated superoxide generation or degranulation activity inflammation in a subject.

Takano, the secondary reference, fails to remedy the deficiencies of Olson. Takano fails to teach or suggest PLD initiated PMN inflammation, let alone a method for modulating or treating a disease or condition associated with PLD initiated PMN inflammation.

Takano fails to teach or suggest, provide any motivation or an expectation of success so that one of ordinary skill in the art would utilize ***any of the lipoxin analogs***, described throughout the application, as pharmaceuticals capable of modulating a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation or for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation or for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity or for treatment of PLD initiated superoxide generation or degranulation activityin a subject.

Takano also fails to teach or suggest, provide any motivation or an expectation of success so that one of ordinary skill in the art would utilize ***any of the lipoxin analogs***, described throughout the application, in ***packaged pharmaceuticals*** with instructions for treatment of a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation or for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation or for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity or for treatment of PLD initiated superoxide generation or degranulation activityin a subject.

Neither reference, alone or in combination teaches or suggests, provides any motivation or an expectation of success so that one of ordinary skill in the art would utilize ***any of the lipoxin analogs***, described throughout the application, as pharmaceuticals capable of modulating a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation or for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation or for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity or for treatment of PLD initiated superoxide generation or degranulation activityinflammation in a subject.

Neither reference, alone or in combination, teaches or suggests, provides any motivation or an expectation of success so that one of ordinary skill in the art would utilize ***any of the lipoxin analogs***, described throughout the application, in ***packaged pharmaceuticals*** with instructions for modulating a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation or for treatment of PLD initiated polymorphoneutrophil (PMN) inflammation or for the modulation of a disease or condition associated with PLD initiated superoxide generation or degranulation activity or for treatment of PLD initiated superoxide generation or degranulation activityin a subject.

It is Applicant's position that the Office Action utilizes the combination of references in view of the present invention in a hindsight analysis, which is not permissible by law. In its simplest form, the Office Action makes the argument that any therapeutic method (and hence a therapeutic agent) that might be known to treat inflammation would make it automatically obvious to treat PLD initiated PMN inflammation. The Office Action fails to provide the motivation why the combination of references would make such a discovery legally obvious. Surely the realization, for example, that a known therapeutic agent could be now used for treatment of PLD initiated PMN inflammation, when it was already known for treatment of inflammation, would result in the non-patentability of that treatment method for any compound. This is not the correct legal standard. No one knew or

appreciated that the compound, in the hypothetical example, could be used for such treatment. This analogy mirrors the present case at hand. The discovery and surprise was that the lipoxin compounds of the invention could be used to treat such PLD initiated PMN inflammation. No one had recognized this relationship prior to the presently claimed subject matter; hence the juxtaposition of the impermissible hindsight analysis and/or use of the Applicant's own specification as a blueprint for obviousness.

This becomes an "obvious to try" analysis which is again, not permissible by law. An Applicant's specification and claims cannot be used as a blueprint to solve a previously unknown problem, and then be used against the Applicant.

Therefore, claims 17-32 are in allowable form. Reconsideration and withdrawal of the pending rejection is respectfully requested.

Obviousness-type Double Patenting

Claims 17-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-32 of pending U.S. Patent Application No. 10/042,043.

Upon Notice of Allowance, Applicant is willing to provide a terminal disclaimer with regard to U.S. Patent Application No. 10/042,043, thereby obviating the basis for this rejection.

Claims 17-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,353,026.

Upon Notice of Allowance, Applicant is willing to provide a terminal disclaimer with regard to U.S. Patent No. 6,353,026, thereby obviating the basis for this rejection.

Conclusion

In view of the foregoing, Applicant submits that all pending claims distinguish over all references cited by the Examiner and respectfully requests that all rejections be withdrawn. The Examiner is invited to telephone the undersigned attorney for Applicant in the event that such communication is deemed to expedite prosecution of this application.

Respectfully submitted,

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Date: March 27, 2003

By: _____

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